

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet

| | Complete if Know | vn | |
|------------------------|------------------|----------|--------------|
| Application Number | 10/549,545 | | |
| Filing Date | May 26, 2006 | | |
| First Named Inventor | Matteucci, Mark | | |
| Art Unit | 1626 | | . |
| Examiner Name | | Reitsang | Shiao |
| Attorney Docket Number | 021305-003900 | US | |

| Examiner | Cite | Document Number | U.S. PATENT DO Publication Date | Name of Patentee or | Pages, Columns, Lines, Where |
|-----------|------|---|----------------------------------|-----------------------------|---|
| Initials* | No.1 | Number Kind Code ^{2 (# known)} | MM-DD-YYYY | Applicant of Cited Document | Relevant Passages or Relevant Figures Appear |
| | AA | US-6,855,695 | 02-15-2005 | Xu et al. | |
| | AB | US-6,656,926 | 12-02-2003 | Borch et al. | |
| | AC | US-6,251,933 | 06-26-2001 | Denny et al. | , |
| | AD | US-6,130,237 | 10-10-2000 | Denny et al. | |
| | AE | US-6,020,315 | 02-01-2000 | Bosslet et al. | |
| | AF | US-5,985,909 | 11-16-1999 | Denny et al. | |
| | AG | US-5,877,158 | 03-02-1999 | Bosslet et al. | |
| | AH | US-5,872,129 | 02-16-1999 | Denny et al. | |
| | Αl | US-5,780,585 | 07-14-1998 | Anlezark et al. | |
| | AJ | US-5,750,782 | 05-12-1998 | Denny et al. | |
| | AK | US-5,703,080 | 12-30-1997 | Nakakura et al. | |
| | AL | US-5,622,936 | 04-22-1997 | Wiessler et al. | |
| | AM | US-5,472,956 | 12-05-1995 | Borch et al. | |
| | AN | US-5,403,932 | 04-04-1995 | Borch et al. | |
| | AO | US-5,306,727 | 04-26-1994 | Borch et al. | |
| | AP | US-5,190,929 | 03-02-1993 | Borch et al. | |
| | AQ | US-4,921,963 | 05-01-1990 | Skov et al. | |
| | AR | US-4,908,356 | 03-13-1990 | Borch et al. | |
| | AS | US-3,652,579 | 03-28-1972 | Hoffer et al. | |
| | AT | US-2005/0043244 A1 | 02-24-2005 | Lin et al. | |
| | AU | US-2004/0254103 A1 | 12-03-2004 | Xu et al. | |
| | ΑV | US-2004/0176332 A1 | 09-09-2004 | Borch et al. | |
| | AW | US-2004/0121940 A1 | 06-24-2004 | De Groot et al. | |
| | AX | US-2003/0130189 A1 | 07-10-2003 | Sender et al. | |
| | AY | US-2003/0096743 A1 | 05-22-2003 | Sender et al. | |
| | ΑZ | US-2003/0050331 A1 | 03-13-2003 | Ng et al. | |
| | ВА | US-2003/0008850 A1 | 01-09-2003 | Borch et al. | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | | | | | |
| | 1 | | | | |

| Examiner Signature | /Rei Tsang Shiao/ (07/21/2008) | Date Considered |
|-----------------------|--------------------------------|--------------------|
| | | |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. \(^1\) Applicant's unique citation designation number (optional). \(^2\) Kind Codes of U.S. Patent Documents at www.uspto.gov or MPEP 901.04. \(^3\) Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). \(^4\) For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. \(^5\) Kind of document \(^5\) Kind of document \(^5\) First anguage Translation is attached. \(^5\)

60917705

PTO/SB/08A (07-06)

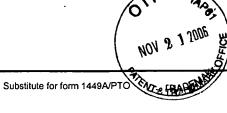
Reitsang Shiao

Complete if Known

10/549,545

May 26, 2006

Matteucci, Mark



INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Sheet

| | | | Art Unit | 1626 |
|---------------------------|--------|----|------------------------|--------------|
| (Use as many sheets as ne | cessar | y) | Examiner Name | Lizzesigned |
| | | 1 | Attorney Docket Number | 021305-00300 |

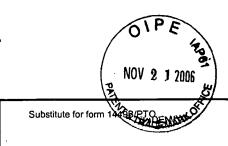
Application Number

First Named Inventor

Filing Date

| | FOREIGN PATENT DOCUMENTS | | | | | | | | | |
|-----------|--------------------------|---------------------------|---|-----------------------------------|------------------|-----------------------------|---|----------------|--|--|
| Examiner | | Cite Foreign Patent Docur | | ocument | Publication Date | Name of Patentee or | Pages, Columns, Lines, Where Relevant Passages | | | |
| Initials* | No.¹ | Country Code ³ | Number ⁴ | Kind Code ⁵ (if known) | MM-DD-YYYY | Applicant of Cited Document | or Relevant Figures Appear | T ⁶ | | |
| | BB | DE | 2229223 | | 02-15-1973 | | | | | |
| | ВС | EP | 648 503 | Al | 04-19-1995 | | | | | |
| | BD | wo | 04/85421 | A2 | 10-07-2004 | | | | | |
| | BE | wo | 04/85361 | Al | 10-07-2004 | | | | | |
| | BF | WO | 02/96910 | Al | 12-05-2002 | , | | | | |
| | BG | wo | 00/64864 | A1 | 11-02-2000 | • | | | | |
| | | | *************************************** | | | | | | | |

| Examiner | /Rei Tsang Shiao/ (07/21/2008) | Date | |
|-----------|--------------------------------|------------|--|
| Signature | /Rei Tsang Shao/ (07/21/2000) | Considered | |
| _ | | 1 | |



INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

3

Sheet

| | Complete if Known | |
|------------------------|-------------------------|----|
| Application Number | 10/549,545 | |
| Filing Date | May 26, 2006 | |
| First Named Inventor | Matteucci, Mark | |
| Art Unit | 1626 | |
| Examiner Name | Unassigned Reitsang Shi | ac |
| Attorney Docket Number | 021305-003900US | |

| NON PATENT LITERATURE DOCUMENTS | | | | | | |
|---------------------------------|---|--|----|--|--|--|
| Examiner Initials * | Unio I managina investa and a second companion and a data page (a) volume icque number(a) nublisher city | | T² | | | |
| | BERRY et al., "5-Nitrofuran-2-ylmethyl group as a potential bioreductively activated pro-drug system," <u>J. Chem. Soc. Perkin Trans.</u> , 1:1147-1156 (1997). | | | | | |
| | ВІ | BORCH et al., "Synthesis and Evaluation of Nitroheterocyclic Phosphoramidates as Hypoxia-Selective Alkylating Agents," J. Med. Chem., 43:2258-2265 (2000). | | | | |
| | BJ | BORCH et al., "Antitumor Activity and Toxicity of Novel Nitroheterocylic Phosphoramidates," J. Med. Chem., 44:74-77 (2001). | | | | |
| | ВK | DE GROOT et al., "Anticancer Prodrugs for Application in Monotherapy: Targeting Hypoxia, Tumor-Associated Enzymes, and Receptors," Current Medical Chemistry, 8:1093-1122 (2001). | | | | |
| | BĽ | DE JAEGER et al., "Relationship of hypoxia to metastatic ability in rodent tumours," Br. J. Cancer, 84(9):1280-1285 (2001). | | | | |
| | ВМ | ENGLE et al., " ³¹ P NMR Kinetic Studies of the Intra- and Intermolecular Alkylation Chemistry of Phosphoramide Mustard and Cognate N-Phosphorylated Derivatives of N, N-Bis(2-chlorethyl)amine ^{1,2} ," J. Med. Chem., 25:1347-1357 (1982). | | | | |
| | BN | EVERETT et al., "Modifying rates of reductive elimination of leaving groups from indolequinone prodrugs: a key factor in controlling hypoxia-selective drug release," <u>Biochemical Pharmacology</u> , 63:1629-1639 (2002). | | | | |
| | во | EVERETT et al., "Bioreductively-Activated Prodrugs for Targeting Hypoxic Tissues: Elimination of Aspirin from 2-Nitroimidazole Derivatives," <u>Biooganic Med. & Chem. Ltrs.</u> , 9:1267-1272 (1999). | | | | |
| • | ВР | HAY et al., "A 2-Nitroimidazole Carbamate Prodrug of 5-Amino-1-(Chloromethyl)-3-[(5,6,7-Trimethoxyindol-2-YL)Carbonyl]-1,2-Dihydro-3 <i>H</i> -Benz[E]Indole (Amino- <i>Seco</i> -CBI-TMI) for Use With Adept and Gdept," Biooganic Med. & Chem. Ltrs., 9:2237-2242 (1999). | | | | |
| | BQ | HAY et al., "Structure-Activity Relationships of 1,2,4-Benzotriazine 1,4-Dioxides as Hypoxia-Selective Analogues of Tirapazamine," <u>J. Med. Chem.</u> , 46:169-182 (2003). | | | | |
| | BR | HERNICK et al., "Design, Synthesis, and Biological Evaluation of Indolequinone Phosphoramidate Prodrugs Targeted to DT-diaphorase," J. Med. Chem., 45:3540-3548 (2002). | | | | |
| | BS | HERNICK et al., "Studies on the Mechanisms of Activation of Indolequinone Phosphoramidate Prodrugs," <u>J. Med. Chem.</u> , 46:148-154 (2003). | | | | |

4

| Examiner Signature | /Rei Tsang Shiao/ (07/21/2008) | Daté Considered | |
|-----------------------|--------------------------------|--------------------|--|
|-----------------------|--------------------------------|--------------------|--|

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered, lockude copy of this form with next communication to applicant.

not considered. Include copy of this form with next communication to applicant.

Applicant's unique citation designation number (optional). Applicant is to place a check mark here if English language Translation is attached.



4

Substitute for form 1449B/PTO

Sheet

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

4

| | Complete if Known | |
|------------------------|-------------------|------|
| Application Number | 10/549,545 | |
| Filing Date | May 26, 2006 | |
| First Named Inventor | Matteucci, Mark | |
| Art Unit | 1626 | |
| Examiner Name | | hiac |
| Attorney Docket Number | 021305-003900US | |

| NON PATENT LITERATURE DOCUMENTS | | | | | | | |
|---------------------------------|--|---|--|--|--|--|--|
| Examiner Initials * | Y''' I | | | | | | |
| | BT KYLE et al., "Direct Assessment of Drug Penetration into Tissue Using a Novel Application of Three-Dimensional Cell Culture," <u>Cancer Research</u> , 64:6304-6309 (2004). | | | | | | |
| | BU | LIN et al., "(o- and p- Nitrobenzyloxycarbobyl) -5-fluorouracil Derivatives as Potential Conjugated Bioreductive Alkylating Agents," J. Med. Chem., 29:84-89 (1986). | | | | | |
| | BV | NAYLOR et al., "Recent Advances in Bioreductive Drug Targeting," Mini Reviews in Med. Chem., 1:17-29 (2001). | | | | | |
| | ВW | PAPOT et al., "Design of Selectively Activated Anticancer Prodrugs: Elimination and Cyclization Strategies," <u>Curr. Med. Chem Anti-Cancer Agents</u> , 2:155-185 (2002). | | | | | |
| •••• | ВX | PARVEEN et al., "2-Nitroimidazol-5-Ylmethyl as a Potential Bioreductively Activated Prodrug System: Reductively Triggered Release of the Parp Inhibitor 5-Bromoisoquinolinone," <u>Biooganic Med. & Chem. Ltrs.</u> , 9:2031-2036 (1999). | | | | | |
| | BY | ROFSTAD et al., "Hypoxia-induced metastasis of human melanoma cells: involvement of vascular endothelial growth factor-mediated angiogenesis," <u>Br. J. Cancer</u> , 80(11):1697-1707 (1999). | | | | | |
| | BZ | ROSEN et al., "Phase 1 Study of TLK286 (Telcyta) Administered Weekly in Advanced Malignancies," Clin. Cancer Res., 10:3689-3698 (2004). | | | | | |
| | CA | STEINBERG et al., "Synthesis and Evaluation of Pteroic Acid-Conjugated Nitroheterocyclic Phosphoramidates as Folate Receptor - Targeted Alkylating Agents," <u>J. Med. Chem.</u> , 44:69-73 (2001). | | | | | |
| ••••• | СВ | WAKSELMAN, M., "1,4- and 1,6- Eliminations from Hydroxy- and Amino-Substituted Benzyl Systems: Chemical and Biochemical Applications," Nouv. J. Chim., 7(7):439-447 (1983). | | | | | |
| | СС | WEST et al., "A comparison of adriamycin and mAMSA, II. Studies with V79 and human tumour multicellular spheroids," Cancer Chemother. Pharmacol., 20:109-114 (1987). | | | | | |
| | CD | WORKMAN et al., "The experimental development of bioreductive drugs and their role in cancer therapy," Cancer and Metastasis Rev., 12:73-82 (1993). | | | | | |

| | | | |
|-----------------------|--------------------------------|--------------------|-------------|
| Examiner Signature | /Rei Tsang Shiao/ (07/21/2008) | Date Considered | |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Applicant's unique citation designation number (optional). Applicant is to place a check mark here if English language Translation is attached.